

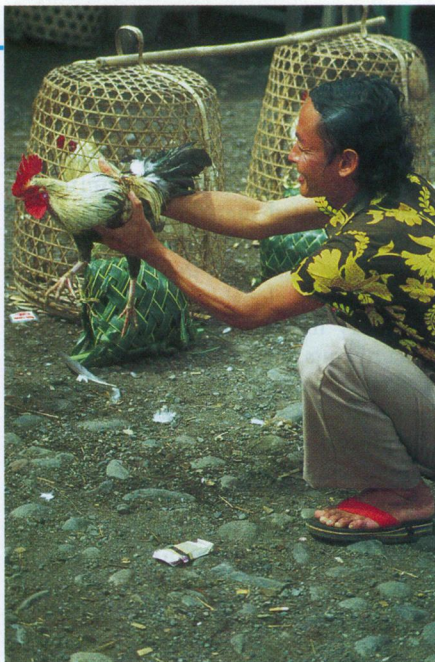
the research has since produced crucial fundamental insights. As researchers zero in on the specific amino-acid sequences that bind with integrins, he says, they've developed a molecular probe for better understanding communication between cells. "When that information transfer becomes dysfunctional," he notes, "it can induce disease states."

Bird Flu Vaccine

In the race to develop vaccines against an ever-widening array of infectious diseases, Aviron, a biopharmaceutical research and development company located in Mountain View, California, may be leading by a nose. Working in collaboration with the National Institutes of Health and the Centers for Disease Control and Prevention, Aviron is developing a novel technology in antiviral vaccinations: the cold-adapted live influenza vaccine. A major advantage of the new technology is that the vaccine may be administered through a nasal spray, bypassing the need for injections. Currently, Aviron is using its technology to develop two candidate vaccines against the avian A/Hong Kong/97 (H5N1) influenza virus, more commonly known as the "bird flu."

The bird flu, which first appeared in humans in May 1997, is the latest in a string of what are known as "Hong Kong flu" epidemics—outbreaks that start in southeast China, where the densely packed population lives cheek to beak with large numbers of chickens, ducks, and other poultry. It is believed that the birds carry various viral strains that are then transmitted somehow—perhaps through pig intermediaries—to humans. Scientists aren't sure why or how the viruses cross over to humans, but the results in the past have been devastating, as evidenced by outbreaks such as one in 1968 that killed thousands worldwide. In December, Hong Kong officials launched what appears to have been a successful strike against the disease by slaughtering over 1 million chickens and other poultry.

Martin Bryant, vice president of research for Aviron, says, "With the elimination of the Hong Kong poultry population, the epidemic was aborted; the virus never got up the steam to pass from one person to another. What happens is that a virus may be modified as it passes from person to person, and that did not occur." Still, says Bryant, although the bird flu didn't spread to epidemic proportions this time, it's not a matter of whether such an epidemic will come, but when—and public health officials should be prepared.



Friend or fowl? A new vaccine technology may prevent outbreaks of the avian A/Hong Kong/97 influenza virus, or "bird flu," which has recently begun to appear in humans.

Aviron scientists are using a "reverse genetics," or recombinant, approach to introduce specific protective genes into an attenuated (weakened) master donor virus strain from which all flu vaccines are developed. The vaccine could also be used as a platform to prepare an inactivated version of the vaccine in large quantities.

Aviron's live-virus vaccines are attenuated viruses that are adapted to grow in the relatively cool nasal region as well as in the lungs. The cold-adapted flu virus triggers an immune response at the place of entry of the influenza virus, leaving the vaccine recipient free of flu but armed with immune capabilities to combat future attacks by the virus.

Exposure to the flu is believed to occur largely through inhalation of droplets containing the live virus, and some view the nasal spray as working directly at the site of infection. In a 1997 trial of 1,602 children aged six years and younger, the nasal spray vaccine showed an amazing 93% efficacy rate against culture-confirmed influenza. This efficacy rate may be due to the fact that spraying the vaccine in the nose stimulates the mucosal antibodies found in the nose, throat, and mouth, and circulating antibodies in the bloodstream. These antibodies are an added boost to the cell-mediated immune responses triggered by the traditional flu shot.

The absence of needles is seen as an advantage in getting the vaccine to people who are afraid of shots, particularly children, who are one of the primary vectors of influenza. Says Bryant, "The first wave of any epidemic in a community usually starts with kids." Plus, because it's a simple nose-

spray, the vaccine wouldn't need to be administered by a health-care professional. Eventually, the vaccine may even be available over the counter.

The Aviron live-virus vaccine is currently undergoing late Phase III trials. The company hopes to present its product for license review by the Food and Drug Administration by mid-1998. Although a bird flu epidemic appears to have been temporarily staved off, Bryant says, "We may not use it this time, but there will be a time when we will. We are working hard to be ready before it comes."

The State of the Science on Endocrine Disruptors

As research on endocrine-disrupting chemicals flourishes worldwide, international groups are working to coordinate research activities being conducted by organizations around the globe. The International Programme on Chemical Safety (IPCS), a collaborative program of the World Health Organization (WHO), the International Labour Organization, and the United Nations Environment Programme, is leading an effort to conduct a global inventory of ongoing research activities related to the health and ecological effects of endocrine-disrupting chemicals, and is working to develop an international assessment of the state of the science on endocrine disruptors. The Organisation for Economic Co-operation and Development (OECD) is leading international efforts on delineating testing methods for endocrine disruptors.

On 16–18 March 1998, the IPCS, in coordination with the OECD, convened a joint meeting in Washington, DC, with a steering committee of scientific experts to provide guidance for these projects. The steering group was made up of representatives from Canada, Finland, Germany, Italy, Sweden, the Netherlands, Mexico, Japan, the United Kingdom, and the United States. The objectives of the meeting were to discuss the structure and content of the global inventory and to define the objectives and scope of the international state of the science assessment document, as well as develop an outline and guidelines for development of the document.

Participants were asked to discuss a working definition for endocrine-disrupting chemicals, and it was agreed to define an endocrine disruptor as an exogenous substance or mixture that alters the function of the endocrine system and consequently causes adverse health effects in an intact organism or its progeny or subpopulations. A potential endocrine disruptor is defined as an exogenous substance or mixture that possesses